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EXAMINER	
KINGAN, TIMOTHY G	

ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/801,361	QUAKE ET AL.	
	Examiner	Art Unit	
	TIMOTHY G. KINGAN	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-92* is/are pending in the application.

4a) Of the above claim(s) *31-50,53-56,60-66 and 70-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,7-30,57,59 and 67-69* is/are rejected.

7)☒ Claim(s) *4,6,51,52 and 58* is/are objected to.

8)☒ Claim(s) *1-92* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/15/2004 and 11/21/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Election of Group I, claims 1-30, 51-52, 57-59 and 67-69 filed on 07/25/08 is acknowledged. In response to the Applicants' traverse of the restriction requirements for Groups I and II, the examiner would like to indicate, as stated in the Requirement for Restriction, that the inventions as claimed have different designs and do not encompass overlapping subject matter. Therefore, the restriction is proper and is made FINAL. Thus, Claims 1-92 are pending in the application, claims 31-50, 53-56, 60-66 and 70-92 are withdrawn from consideration as directed to non-elected inventions, and claims 1-30, 51-52, 57-59 and 67-69 are considered on the merits.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-30, 51, 52, 57-59 and 67-69 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 10-25, 46-47, 52-53 and 61-63 of U.S. Patent No. 7,351,376. Although the conflicting claims are not identical, they are not patentably distinct from each other because the elements of the independent and dependent claims of the instant application are found in the corresponding claims of U.S. '376. The elements of individual claims of the instant application are found in their entirety in corresponding claims of U.S. '376 or the are found in combinations of independent and dependent claims of U.S. '376, with the dependencies revealing equivalent subject matter, or they are found in combinations of dependent claims, again, with the dependencies revealing claims of equivalent subject matter. The elements of the claims found in U.S. '376 include a microfluidic device with a loop and service channel (with inlet and outlet), a microvalve, made from elastomeric material, a pump and target molecules disposed in the loop channel. The correspondence between claims of the instant application and those of U.S. '376, with the latter in parentheses, are as follows: 1 (1), 2 (2), 3 (1), 4 (1+2), 5 (3), 6 (1+3), 7 ((4), 8 (5), 9 (6), 10 (7), 11 (8+11), 12 (10), 13 (10+1), 14 (10+1). 15, (11), 16 (12), 17 (8+13), 18 (13), 19 (14), 20 (15), 21 (16), 22 (17), 23 (18), 24 (19), 25 (20), 26 (21), 27 (22), 28 (23), 29 (24), 30 (25), 51 (46), 52 (47), 57 (52), 58 (52), 59 (53), 67 (61), 68 (62), 69 (63).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. **Claims 1-3, 57, 59 and 67-69** are rejected under 35 U.S.C. 103(a) as being unpatentable over C.J. Backhouse, U.S. Patent 6,318,970 (herein after Backhouse). For Claim 1, Backhouse teaches microfluidic devices for use in biochemical analyses (col 1, lines 8-10) comprising a loop channel intersecting with a main channel (service channel) and a pump associated with the loop channel driving fluid in circulation (col 5, lines 24-55; Figs. 9A-9E). Backhouse does not teach a valve associated with the loop channel; valves associated with microfluidic channels are known in the art, and Backhouse teaches such valves at the junctions of microchannels (col 4, lines 56-57). It would have been obvious to one of ordinary skill in the art to include a valve according

to the teaching of Backhouse at the intersection of the loop and main (service) channels of Backhouse, in order to provide for free flow within the loop channel without loss to the main channel.

For Claim 2, Backhouse teaches microfluidic devices with openings for sample delivery (col 1, lines 28-30; col 6, lines 60-62). It would have been obvious to one of ordinary skill in the art to use an inlet and outlet associated with a service channel in order to provide for sample introduction.

For Claim 3, Backhouse teaches a pump operating by sequential strengthening and weakening of electromagnets to affect a peristaltic movement of fluid (col 3, lines 61-65).

For Claims 57, 59, and 67-69 Backhouse does not teach a plurality of loop channels, each with an associated pump and disposed with target molecules, in a device. It would have been obvious to one of ordinary skill in the art to use multiple loop channels in order to provide for replicate reaction chambers with their associated determinations or to provide for chambers capable of supporting different reactions. Further, it would have been desirable to use loop channels in numbers of 96, 384 or 1536 in order to provide for either supply of samples or collection of reaction products with standard and robotic liquid handling instruments that are commonly configured with modular pipettors arrayed for microtiter plates with 96, 384 or 1536 wells.

6. **Claims 5 and 7-30** are rejected under 35 U.S.C. 103(a) as being unpatentable over Backhouse as applied to claim 1 above, and further in view of R.J. Lipshutz et al., U.S. Patent 6,043,080 (herein after Lipshutz).

For Claims 5 and 7, Backhouse does not teach target molecules disposed in the loop channel. Such immobilizations in microfluidic devices are known in the art; Lipshutz teaches microfluidic devices with arrays of nucleic acid probes immobilized on a substrate (col 10, lines 5-14). It would have been obvious to one of ordinary skill in the art to use the target molecules of Lipshutz in the loop channel of Backhouse in order to provide for a binding or hybridization zone that provides the advantages of kinetics in binding associated with mixing and continuous flow across the sensing surface.

For Claims 8 and 9, Backhouse does not teach proteins or antibodies bound to the loop channel. It would have been obvious to one of ordinary skill in the art to immobilize proteins in such loop in order to provide a means of assaying for protein binding events, just as for nucleic acid hybridization events in the teaching of Lipshutz,, such immobilization and binding occurring in a small volume reaction chamber, the sensitivity of detection for which increases with increasing concentration of bound form in the small volumes associated with such channels.

For Claims 10-12, Backhouse does not teach a loop channel as a detection region, a detector associated with such region and a loop channel comprising an elastomeric material. Lipshutz teaches analytical chambers for detection of nucleic acid hybridization (col 11, lines 38-40) (detection region), such chambers having a transparent window (col 19, lines 22-24) (adjacent to a substrate for detection of

hybridization). It would have been obvious to one of ordinary skill in the art to include a window for detection in the device of Backhouse in order to provide visual confirmation of mixing or reaction within the loop channel. Further, it would have been obvious to one of ordinary skill to use a deformable material such as an elastomer in order to provide a material that is readily fabricated with conventional micromachining of photolithographic methods.

For Claims 13 and 14, Backhouse does not teach a valve associated with the loop channel or formed of an elastomer; valves associated with microfluidic channels are known in the art, and Backhouse teaches such valves at the junctions of microchannels (col 4, lines 56-57). Lipshutz teaches microfluidic devices (comprising valves) may be fabricated from suitable polymers including Teflon (an elastomer) (col 15, lines 44-53). It would have been obvious to one of ordinary skill in the art to use an elastomeric material for channels and valves in order to provide a material that will deform and return to shape when pumping material of varying viscosities or the presence of particulates.

For Claims 15-18, Backhouse does not teach a detection region in the loop channel. Lipshutz teaches microfluidic devices comprising analytical chambers for detection of nucleic acid hybridization (col 11, lines 38-40) (detection region), such chambers having a transparent window (col 19, lines 22-24) (adjacent to a transparent substrate for detection of hybridization) and that such devices may be fabricated from suitable polymers including Teflon (an elastomer) (col 15, lines 44-53). It would have been obvious to one of ordinary skill in the art to use a transparent material for a

detection region in order to provide for an optimal detection and resolution of particulate materials.

For Claims 19-23, Backhouse teaches loop and main channels in a layer (col 5, lines 24-55; Figs. 9A-9E) (treatment layer). Backhouse does not teach separate control and treatment layers, the control layer carrying control lines. Lipshutz teaches microfluidic devices may be formed by lamination of one set of parts to another (formation of layers, e.g., treatment and control layers, bonded to each other), resulting in interconnection of fluid channels (col 15, lines 35-43) (channels in control layer carrying control lines intersecting with channels in treatment layer), that such devices may be fabricated from suitable polymers including Teflon (an elastomer) (col 15, lines 44-53) and detection regions comprise a transparent window (col 19, lines 22-24) (a treatment or control layer is transparent). It would have been obvious to one of ordinary skill in the art to use such layered substrate in order to facilitate fabrication of modules by simplifying the individual components of the assembled structure.

For Claim 24, Backhouse and Lipshutz do not teach an intersection of layers comprising channels forming a microvalve. It would have been obvious to one of ordinary skill in the art to that such intersections be fitted with a valve in order to provide for delivery of reagents, for instance to a hybridization site according to the teaching of Lipshutz with subsequent isolation of the reaction chamber to prevent mixing with reagent in channels adjacent to reaction chamber.

For Claim 25, Backhouse does not teach deformable valves between treatment and control channels. Lipshutz teaches valve structures in microfluidic devices

incorporating a membrane or diaphragm which may be deflected onto a valve seat (col 29, lines 64-66) (deformable membrane). It would have been obvious to one of ordinary skill in the art to use such membrane or deformable material as a valve between the laminated or layered structures of Lipshutz in order to provide the advantages associated with simple mechanical deformation of a membrane for closing off a channel.

For Claims 26 and 27, Backhouse does not teach supply of control channels with pressurized fluid or air. Lipshutz teaches the use of pressure differentials provided to various reaction chambers of the device, incorporating pressure inlets connecting the reaction chamber to the pressure source (positive or negative) (col 21, lines 21-30) (supplied with a pressurized fluid). It would have been obvious to one of ordinary skill in the art to use a gas such as air for such positive pressure source in the device of Backhouse in order to attain the advantages of a readily available source of pressure and that can be controlled in small increments with respect to pressure and duration of application, that is generally inert in its reactivity and avoids the potential for mixing with fluid drive materials

For Claim 28, Backhouse and Lipshutz do not teach a transparent substrate and an adjacent and transparent treatment or control layer. Lipshutz teaches a reaction chamber having a transparent window (col 19, lines 22-24). It would have been obvious to one of ordinary skill in the art to use a transparent material for a detection region in the device of Backhouse in order to provide for an optimal detection and resolution of particulate materials.

For Claim 29, Backhouse does not teach a loop channel as a detection region, a detector associated with such region and a loop channel comprising an elastomeric material. Lipshutz teaches analytical chambers for detection of nucleic acid hybridization (col 11, lines 38-40) (detection region), such chambers having transparent windows (col 19, lines 22-24) (adjacent to a substrate for detection of hybridization). It would have been obvious to one of ordinary skill in the art to use a detection region in the loop channel of the devices for biochemical analysis of Backhouse (col 1, lines 8-10) in order to provide for use of optical detection methods in such analyses.
For Claim 30, Backhouse teaches circular loop channels (col 5, lines 20-21; Figs. 9A-E).

Allowable Subject Matter

7. **Claims 4, 6, 51, 52 and 58** are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. No prior art of record teaches or fairly suggests pumps comprising at least three microvalves and combinations of parallel and anti-parallel channels associated with loop channels.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY G. KINGAN whose telephone number is (571)270-3720. The examiner can normally be reached on Monday-Friday, 8:30 A.M. to 5:00 P.M., E.S.T..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

10/27/2008

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

TGK